FENWICK & WEST LLP

SAN FRANCISCO OFFICE | EMBARCADERO CENTER WEST
275 BATTERY ST., SUITE 1500 | SAN FRANCISCO, CA 94111
TEL 415.875.2300 | FAX 415.281.1350 | WWW.FENWICK.COM

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CONFIDENTIAL

DATE: March 4, 2004

CLIENT-MATTER NO.: 23546-07665
Isis Ref. RTS-275

TO:

NAME	FAX NO.	PHONE NO.
Examiner McGarry Group Art Unit No. 1635 U.S. Patent and Trademark Office	703-872-9306	

FROM: Susan T. Hubl, Ph.D. **PHONE:** (415) 875-2316

SENT BY: Cheryl Leger **PHONE:** (415) 875-2495

RE: In Re: Application No. 10/006,191

NUMBER OF PAGES WITH COVER PAGE: 7	ORIGINAL WILL NOT FOLLOW

MESSAGE:

Please see attached Response to Restriction Requirement and Preliminary Amendment.

0001/PTO Rev. 10/95 — U.S. Department of Commerce Patent and Trademark Office			
TRANSMITTAL FORM *(to be used for all correspondence during pendency of filed application)*		Application Number	10/006,191
		Filing Date	December 10, 2001
		First Named Inventor	William Gaarde
		Group Art Unit Number	1635
		Examiner Name	Sean McGarry
Total Number of Pages in This Submission	7	Attorney Docket Number	23546-07665 (RTS-274)

ENCLOSURES *(check all that apply)*

- ☐ Fee Transmittal Form (In duplicate)
  - ☐ Check Enclosed
- ☐ Return Receipt Postcard
- ☐ Response to Notice to File Missing Parts
- ☐ Assignment & Recordation Cover Sheet
- ☐ Declaration
- ☐ Power of Attorney
- ☐ Application Data Sheet
- ☐ Information Disclosure Statement & PTO/SB/08A
  - ☐ Copies of IDS Cited References
- ☐ Request for Corrected Filing Receipt
- ☐ Request for Correction of Recorded Assignment
- ☒ Response to Restriction Requirement and Preliminary Amendment: [5] Page(s)
  - ☐ After Final
- ☐ Status Request
- ☐ Revocation and Substitute Power of Attorney
- ☐ Issue Fee Transmittal
- ☐ Letter to Chief Draftsperson
- ☐ Formal Drawing(s):
  [ ] Sheet(s) of Figure(s) [ ]
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Certified Copy of Priority Document(s)
- ☐ After Allowance Communication to Group
- ☒ Fax Cover Page
- ☐ _____
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REMARKS:

SIGNATURE OF ATTORNEY OR AGENT

Signature:			
Attorney/Reg. No.:	Susan T. Hubl, Ph.D., Patent Agent, 47,668	Dated:	March 4, 2004

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I hereby certify that this correspondence, including the enclosures identified above, is being transmitted on the date shown below via facsimile to: Commissioner for Patents at the facsimile number indicated below.

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Facsimile Number:	1-703-872-9306		

IN THE UNITED STATES
PATENT AND TRADEMARK OFFICE

APPLICANT(S):	GAARDE ET AL
APPLN NO.:	**10/006,191**
FILING DATE:	12/10/2001
TITLE:	ANTISENSE MODULATION OF CONNECTIVE TISSUE GROWTH FACTOR EXPRESSION
EXAMINER:	MCGARRY
GAU:	1635
ATTY. DKT. NO.:	23546-07665/US (RTS-274)

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Dated: March 4, 2004 By: Susan T. Hubl

Susan T. Hubl, Ph.D., Reg. No.: 47,668

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RESPONSE TO RESTRICTION REQUIREMENT

AND PRELIMINARY AMENDMENT

SIR:

Responsive to the Office Action dated February 5, 2004 received in the above-identified patent application, please enter the following amendments, and consider the accompanying remarks.

Amendments to the Claims begin on page 2. **Remarks** begin on page 4.

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A compound 8 to 50 nucleobases in length targeted to a 3'UTR of a nucleic acid molecule encoding connective tissue growth factor (SEQ ID NO:19), wherein said compound specifically hybridizes with said nucleic acid molecule encoding connective tissue growth factor and inhibits the expression of connective tissue growth factor.

2. (Original) The compound of claim 1 which is an antisense oligonucleotide.

3. (Currently amended)The compound of claim 2 wherein the antisense oligonucleotide has a sequence comprising SEQ ID NO: ~~24, 25, 27, 28, 33, 34, 35, 36, 38, 39, 41,~~ 45, 46, 47, 48, ~~50, 52, 58,~~ 62, 63, or 64, ~~68, 70, 72, 73, 81, 86, 88, 90, 91, 92, 95, 97, 30, 31, 32, 37, 40, 42, 103, 104, 106, 108, 110, 111, 116, 117, 120, 122, 124, 126, 127, 128, 130, 134, 135, 136, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 151 or 153~~.

4. (Original) The compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage.

5. (Original) The compound of claim 4 wherein the modified internucleoside linkage is a phosphorothioate linkage.

6. (Original) The compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified sugar moiety.

7. (Original) The compound of claim 6 wherein the modified sugar moiety is a 2'-O-methoxyethyl sugar moiety.

8. (Original) The compound of claim 2 wherein the antisense oligonucleotide comprises at least one modified nucleobase.

9. (Original) The compound of claim 8 wherein the modified nucleobase is a 5-methylcytosine.

10. (Original) The compound of claim 2 wherein the antisense oligonucleotide is a chimeric oligonucleotide.

11. (Original) A compound 8 to 50 nucleobases in length which specifically hybridizes with at least an 8-nucleobase portion of an active site on a nucleic acid molecule encoding connective tissue growth factor.

12. (Original) A composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier or diluent.

13. (Original) The composition of claim 12 further comprising a colloidal dispersion system.

14. (Original) The composition of claim 12 wherein the compound is an antisense oligonucleotide.

15. (Withdrawn) A method of inhibiting the expression of connective tissue growth factor in cells or tissues comprising contacting said cells or tissues with the compound of claim 1 so that expression of connective tissue growth factor is inhibited.

16. (Withdrawn) A method of treating an animal having a disease or condition associated with connective tissue growth factor comprising administering to said animal a therapeutically or prophylactically effective amount of the compound of claim 1 so that expression of connective tissue growth factor is inhibited.

17. (Withdrawn) The method of claim 16 wherein the disease or condition is a hyperproliferative disorder.

18. (Withdrawn) The method of claim 17 wherein the hyperproliferative disorder is cancer.

19. (Withdrawn) The method of claim 18 wherein the cancer is selected from the group consisting of breast, prostate and renal cancer.

20. (Withdrawn) The method of claim 16 wherein the disease or condition is selected from the group consisting of pulmonary fibrosis, renal fibrosis, scleroderma, and atherosclerosis.

REMARKS

STATUS OF THE CLAIMS

Claims 1-20 were pending in this application. Claims 15-20 have been withdrawn without prejudice. Claims 1 and 3 have been amended. Following entry of the amendments claims 1-15 will be pending and at issue.

SUPPORT FOR AMENDMENTS TO THE CLAIMS

Claim 1 has been amended to include the terms "3' UTR" and "SEQ ID NO:19" to more clearly define Applicant's invention. Support for the term "3' UTR" can be found throughout the specification as filed, e.g., page 15, paragraph 2. Support for the term "SEQ ID NO:19" can be found throughout the specification as filed, e.g., Example 15 including Table I on pages 91-93.

Claim 3 has been amended to recite the SEQ ID NOS of only those oligonucleotides that hybridize to the 3'UTR of target SEQ ID NO:19 and inhibit the expression of connective tissue growth factor. Support for this amendment to claim 3 is found throughout the specification as filed, e.g., Example 15 including Table I on pages 91-93.

The amendments to the claims therefore add no new matter.

ELECTION/RESTRICTION REQUIREMENT

The Examiner has required restriction of the claims to Group I (claims 2-14 drawn to compounds) and Group II (claims 15-20, drawn to methods of treating disease)

In response, Applicant elects Group I (claims 2-14) without traverse. Applicant has herein withdrawn claims 15-20.

The Examiner has also required election of one (1) antisense sequence from claim 3. The Examiner notes that Claim 1 links the inventions recited in claim 3, and the restriction requirement among the linked inventions is subject to the non-allowance of linking claim 1. Upon the allowance of linking claim 1, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application.

In response, Applicant elects without traverse SEQ ID NO:48 of claim 3.

CONCLUSION

Reconsideration of the claims is respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (415) 875-2316.

Respectfully submitted,
GAARDE ET AL

Dated: March 4, 2004

By: _____

Susan T. Hubl, Ph.D. Patent Agent
Reg. No.: 47,668
Fenwick & West LLP
Silicon Valley Center
801 California Street
Mountain View, CA 94041
Tel.: (415) 875-2316
Fax.: (650) 938-5200